Express Mail No.:
EV 335 857 110 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Tucker et al.

Application No.: 09/813,214

Confirmation No. 1989

Filed: March 3, 2001

Group Art Unit: 1645

For: *MORAXELLA CATARRHALIS* OUTER MEMBRANE PROTEIN-106 POLYPEPTIDE, GENE SEQUENCE AND USES THEREOF

Examiner: Shahnan Shah, Khatols

Attorney Docket No.: 7969-089

DECLARATION OF KENNETH D. TUCKER AND LAURA A. PLOSILA UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, KENNETH D. TUCKER and LAURA A. PLOSILA do declare that:

1. We are the sole co-inventors of the invention of claims 1-8, 11-12, 19, 21, 34 and 42-56 in the above-identified application, which we understand to be divisional of an earlier filed application no. 08/968,685 filed Nov. 12, 1997 which, in turn, is a continuation-in-part of our earlier application No. 08/642,712 filed May 3, 1996 (Grand-Parent Application).

2. Attached as Exhibits A1 and A2 are: 1) a copy of claims 1-8, 11-12, 19, 21, 34 and 42-56 which we understand will be pending upon entry of an Amendment being submitted with this Declaration (Exhibit A1); and 2) a copy of the Grand Parent Application filed May 3, 1996 (Exhibit A2).

3. We conceived and completed the invention of claims 1-8, 11-12, 19, 21, 34 and 42-56, first described and claimed in the Grand Parent application, filed May 3, 1996,

which encompasses isolated OMP106 polypeptide, fragments thereof, vaccine containing the isolated OMP 106 polypeptide or fragment thereof and method of producing an immune response to said polypeptide and fragments, before April 1, 1995. This is evidenced by the facts described below and the evidence in the attached exhibits.

4. Attached are Exhibits B-F which are copies of documents that report and describe work done by us or under our direction and supervision in the United States.

5. We have reviewed each of the documents shown in Exhibits B-F. Although the dates have been redacted, each date of the documents shown in Exhibits B-F is before April 1, 1995.

6. Exhibit B is a copy of a page from the laboratory notebook of a MicroCarb[1] (Antex Biologics) scientist. This page reports the identification of two outer membrane proteins (OMPs) that are unique to strains of *M. catarrhalis* (i.e., strains 49143 and 25238). The note at the bottom of the page states "2 unique major proteins are seen ... in both 49143 and 25238 (both of which agglutinate human RBC)." The position of each of these "unique" OMPs in the stained gel of the polyacrylamide gel electrophoresis (PAGE)-separated proteins is identified by an arrow with the word "unique" at the right-hand side of the left gel. The gels clearly show that the larger "unique" OMP has a molecular weight much greater than that of the 106 kD molecular weight standard included in the PAGE. This OMP was subsequently designated OMP106.

7. Exhibit C is a copy of a page from the laboratory notebook of an Antex Biologics scientist. This page was recorded after the page shown in Exhibit B was recorded. This page shows the results of a purification procedure that yielded essentially just three OMPs

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from a cultivar of *M. catarrhalis* strain 49143 (see leftmost lane of the gel on the page). The highest molecular weight protein present in the leftmost lane is OMP106. The PAGE separated OMP106 from the other two OMPs produced by the purification procedure. The OMP106 band can be sliced from the gel to yield a pure preparation of OMP106 polypeptide. The results reported on this page evidence our isolation of the OMP106 polypeptide.

8. Exhibit D is a copy of a letter with enclosure from Dr. James K. Noël of HRP, Inc. to one of us, Kenneth D. Tucker. In the letter, Dr. Noël acknowledges receipt of two immunogenic preparations for use in animal immunizations. Accompanying the letter is an immunization schedule, which identifies one of the immunogenic preparations as comprising OMP106 polypeptide, and indicates the animal host to be NZW rabbits.

9. Exhibit E contains a copy of two pages from the laboratory notebook of an Antex Biologics scientist. These pages were recorded after the date of the letter shown in Exhibit D. They report an experiment that used Western blotting to characterize the reactivity of rabbit antisera prepared by HRP scientists using the two immunogenic preparations discussed in paragraph 7, above. The experimental results summarized on notebook page 61 state, *inter alia*, that the antisera K115 "shows reaction with its antigen (i.e., 106) ...." The documents contained in Exhibits C and D evidence our preparation and use of an immunogenic preparation comprising isolated OMP106 polypeptide.

10. Exhibit F is a copy of two pages of a laboratory notebook of an Antex Biologics scientist who worked under our direction or supervision. These pages report determination of the molecular weight of the OMP106 polypeptide isolated from *Moraxella catarrhalis* (a/k/a *Branhamella catarrhalis*) using n-octyl β-D-glucopyranoside (OG). See, in particular, "Purpose" and "Methods" on page 1 of Exhibit F. As indicated, either boiled or not boiled OG extracted OMP106 polypeptide was run on a Tris-Glycine denaturing polyacrylamide

gel electrophoresis (SDS-PAGE) gel together with a variety of molecular weight standards, including Bio-Rad Pre-Stained Standards ranging from 20,700 to 139,900 D (designated Low); Novex Standards ranging from 36,000 to 250,000 D and Bio-Rad Silver Standards ranging from 66,200 to 200,000 D (designated Broad). A copy of a scan of the gel obtained is attached to page 2 of Exhibit F. The molecular weight markers are indicated at the right and top of the band in the scan of the gel. OMP106 is indicated by the arrow in Lanes 3 and 7 in which the boiled OG extracted OMP106 was run.[1] The gel clearly shows that the OMP106 has a molecular weight of about 180 to 230kD. See, in particular, the "Conclusion" on page 2 of Exhibit A which states that the "size of the OMP106 is approximately 200kDA".

11. Based on the evidence presented in Exhibits B-F, we have demonstrated our conception and completion of the presently claimed invention which encompasses isolated OMP106 polypeptides, fragments and a vaccine and method of producing an immune response to said polypeptides and fragments before April 1, 1995. Attention is directed especially to Exhibits D and E. As clearly shown, in Exhibit D, prior to April 1, 1995, we had forwarded to Dr. Noel of HRP, Inc. an immunogenic composition comprising isolated OMP106 of *M.catarrhalis* with an immunization schedule for use to induce an immune response in an animal model, i.e. NZW rabbit. As clearly stated demonstrated in Exhibit E, prior to April 1, 1995, we

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1 It is noted that unboiled OG extract containing OMP106 does not enter the gel (Lanes 2 and 5). See Specification of the Grand Parent Application at page 44, line 30 through page 45, line 17.

had obtained evidence that our isolated OMP106 preparation was useful as an immunogenic preparation to induce an immune response against *M. catarrhalis*. This evidence also demonstrates our invention of vaccine compositions comprising isolated OMP106 as well.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: Oct 1, 2003 Kenneth D Tucker
KENNETH D. TUCKER

Dated: _____
LAURA A. PLOSILA

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Dated:_____

KENNETH D. TUCKER

Dated: 10/4/03 Laura A. Plosila

LAURA A. PLOSILA

Listing of Claims

Please amend the claims to read as set forth in the Listing of the Claims below:

1. (original) An isolated or substantially pure OMP106 polypeptide, which is an outer membrane polypeptide of *Moraxella catarrhalis*, and has a molecular weight of about 180 kD to about 230 kD as determined in SDS polyacrylamide gel electrophoresis using rabbit skeletal muscle myosin and *E. coli* β-galactosidase as the 200 kD and 116.25 kD molecular weight standards, respectively.

2. (original) The OMP106 polypeptide of claim 1, which has a molecular weight of about 190 kD.

3. (original) The OMP106 polypeptide of claim 1, which is an outer membrane polypeptide of *Mōraxella catarrhalis* strain selected from the group consisting of ATCC 25238, ATCC 25240, ATCC 43617, ATCC 43618, ATCC 43627, ATCC 43628 and ATCC 49143.

4. (original) The OMP106 polypeptide of claim 3, which *Moraxella catarrhalis* strain is ATCC 49143.

5. (original) The OMP106 polypeptide of claim 3, wherein the *Moraxella catarrhalis* is a hemagglutinating cultivar.

6. (original) The OMP106 polypeptide of claim 1, which reacts with silver stain.

7. (previously presented) The OMP106 polypeptide of claim 1, which specifically binds an antibody that specifically binds the sequence of SEQ ID NO:1.

8. (previously presented) The OMP106 polypeptide of claim 1, which specifically binds an antibody that specifically binds the sequence of SEQ ID NO: 11.

9.-10. Cancelled.

11. (previously presented)The OMP106 polypeptide of claim 1, which comprises the sequence of SEQ ID NO:1.

12. (previously presented) The OMP106 polypeptide of claim 11, which additionally comprises the sequence of SEQ ID NO: 11.

13. (withdrawn) An isolated antibody that specifically binds the OMP106 polypeptide of claim 1 or a fragment thereof.

14. (withdrawn) An isolated antibody that specifically binds the OMP106 polypeptide of claim 9 or a fragment thereof.

15. (withdrawn) An isolated antibody that specifically binds the OMP106 polypeptide of claim 11 or a fragment thereof.

16. (withdrawn) The isolated antibody of claim 13 or 14, which is a cytotoxic antibody that mediates complement killing of *Moraxella catarrhalis*.

17.-18. Cancelled.

19. (previously presented) A vaccine comprising the OMP106 polypeptide of any of claims 1, 2, or 5.

20. Cancelled.

21. (previously presented) An antigenic composition comprising the OMP106 polypeptide of any of claims 1, 2, or 5.

22.-26. Cancelled.

27. (withdrawn) A method of producing an immune response in an animal comprising immunizing the animal with an effective amount of the OMP106 polypeptide of any of claims 1, 2, or 5.

28. Cancelled.

29. (withdrawn) A method of producing a non-hemagglutinating cultivar of *M. catarrhalis* from a HA *M. catarrhalis* strain or cultivar, which comprises serially passaging a HA *M. catarrhalis* strain or cultivar in static liquid cultures.

30.-33. Cancelled.

34. (Amended) An isolated or substantially pure OMP106 polypeptide which comprises the sequence of SEQ ID NO:10.

35. (withdrawn) An isolated antibody that specifically binds the OMP106 polypeptide of claim 33 or a fragment thereof.

36.-39. Cancelled.

40. (withdrawn) A method of producing an immune response in an animal comprising immunizing an animal with an effective amount of the OMP106 polypeptide of claim 34.

41. Cancelled.

42. (previously presented) A vaccine comprising the OMP106 polypeptide of any one of claims 1-6.

43. (previously presented) A vaccine comprising the OMP106 polypeptide of any one of claims 7, 8, 11 or 12.

44. (previously presented) An antigenic composition comprising the OMP106 polypeptide of any one of claims 1-6 and a pharmaceutically acceptable carrier.

45. (previously presented) An antigenic composition comprising the OMP106 polypeptide of any one of claims 7, 8, 11 or 12 and a pharmaceutically acceptable carrier.

46. (previously presented) A vaccine comprising the OMP106 pol ypeptide of any one of claims 1-6 and an adjuvant.

47. (previously presented) A vaccine comprising the OMP106 polypeptide of any one of claims 7, 8, 11 or 12 and an adjuvant.

48. (previously presented) A vaccine comprising the OMP106 polypeptide of claim 34.

49. (previously presented) A vaccine comprising the OMP106 polypeptide of claim 34 and an adjuvant.

50. (previously presented) An antigenic composition comprising the OMP106 polypeptide of Claim 34.

51. (previously presented) An antigenic composition comprising the OMP106 polypeptide of Claim 34 and a pharmaceutically acceptable carrier.

52. (previously presented) The OMP106 polypeptide of claim 1, which specifically binds an antibody that specifically binds the sequence of SEQ ID NO. 10.

53. (previously presented) An antigenic composition comprising the OMP106 polypeptide of claim 52.

54. (previously presented) An antigenic composition comprising the OMP106 polypeptide of claim 52 and a pharmaceutically acceptable carrier.

55. (previously presented) A vaccine comprising the OMP106 polypeptide of claim 52.

56. (previously presented) A vaccine comprising the OMP106 polypeptide of claim 52 and an adjuvant.